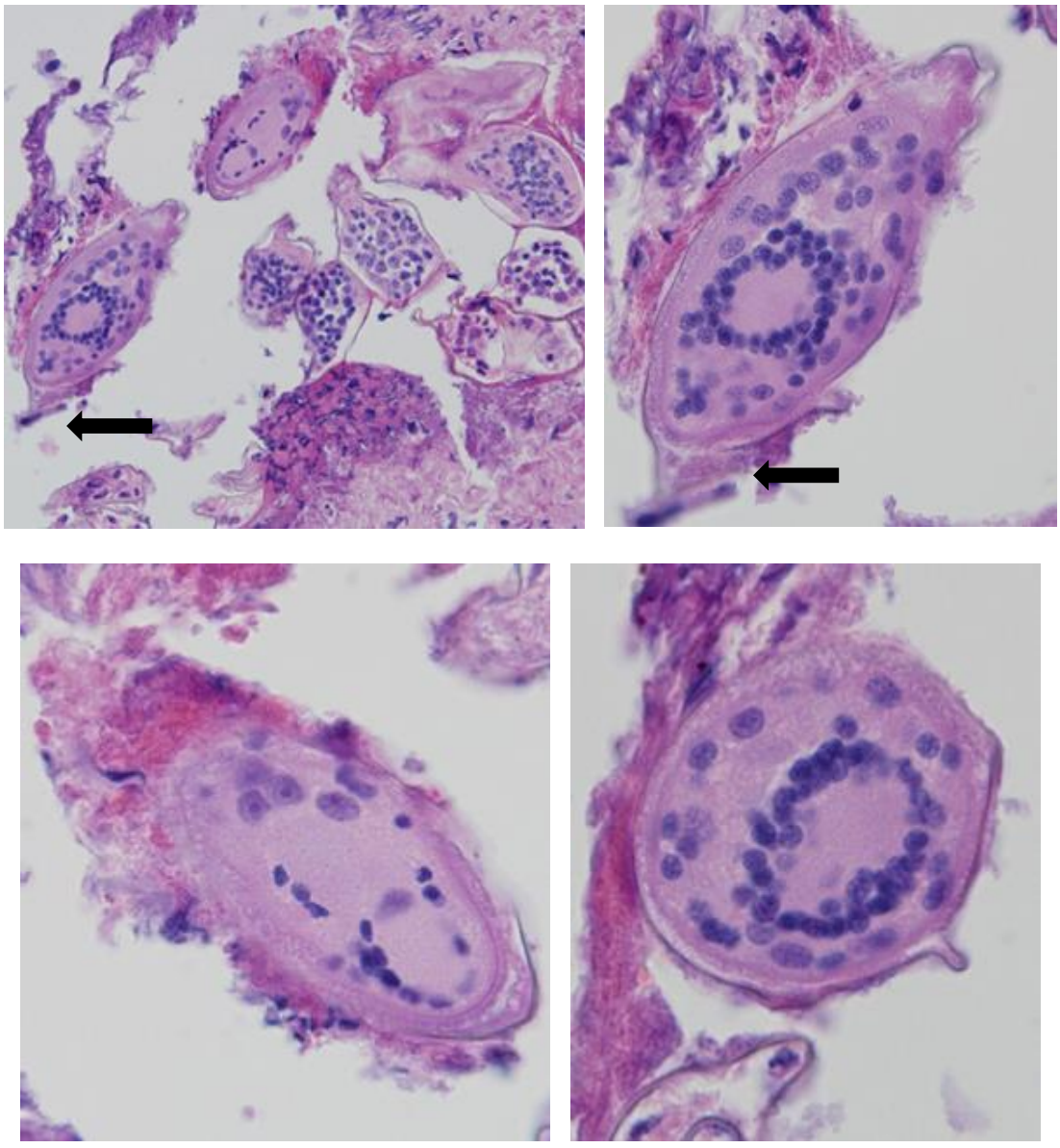
PARASITOLOGY CASE HISTORY 7 (HISTOLOGY)
(Lynne S. Garcia)

A 55 year-old female presented with cervical carcinoma. Her history indicated she had lived most of her life in Africa. CT scans of the pelvis revealed a small mass in the bladder. Biopsy specimens were submitted for examination. Subsequent microscopy revealed structures that were interpreted as a possible parasite. Routine hematoxylin and eosin stained sections are seen below:



Courtesy of CDC, Washington, DC and John H. Stroger Jr. Hospital, Cook County, Chicago, IL.

- Based on these images, what is your diagnosis?

Scroll Down for Answer and Discussion

Answer and Discussion of Histology Quiz #7

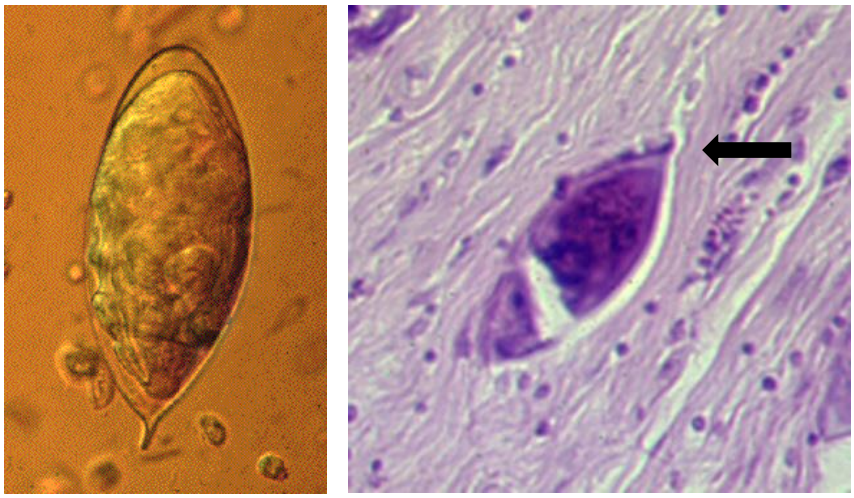
This is a case of schistosomiasis caused by *Schistosoma haematobium*. The images demonstrate the presence of eggs in bladder tissue. Note the terminal spine indicated by the arrows; the eggs contain a miracidium larva.

Schistosomes belong to the phylum Platyhelminthes, family Schistosomatidae**,** and are a group of digenetic, dioecious trematodes requiring definitive and intermediate hosts to complete their life cycles. Four species are important agents of human disease: *Schistosoma mansoni*, *S. japonicum*, *S. mekongi*, and *S. haematobium. S. intercalatum* is of less epidemiologic importance. Schistosomiasis affects between 200 million and 300 million people in 77 countries throughout the world and is a significant cause of disease in areas of endemic infections. In Egypt, approximately 20% of the population is infected; prevalence rates in some villages have been estimated to be 85%. The number of infected individuals in China is estimated to be 1.52 million. Although only about 10% of infected people have serious disease, this represents 20 million to 30 million individuals worldwide. Approximately half of the remaining 180 million to 270 million infected individuals have symptoms.

The earliest known instance of schistosomiasis was found in Egyptian mummies of the predynastic period (3100 BC), using enzyme-linked immunosorbent assay (ELISA) to detect circulating anodic antigen. Previously, eggs were detected in the kidneys of mummies from the Twentieth

Dynasty (1250 BC to 1000 BC). Schistosome infections in the New World probably began with the African slave trade in the Americas during the 16th and 17th centuries.

Humans are the only significant reservoir hosts of *S. haematobium*. Fully embryonated eggs without an operculum (112 to 170 µm by 40 to 70 µm) escape from the body in the urine. The eggs are light yellowish brown and contain a conspicuous terminal spine.



Eggs in bladder; note the terminal spine (lower end in left image – iodine stain, upper end in right image – H & E stain).

The adult male worm contains minute integumentary tuberculations, smaller than those found on adult *S. mansoni* males. *S. haematobium* adults reside in the vesical and pelvic plexuses of the venous circulation. The adult female can contain 20 to 100 eggs in the uterus at one time. In addition to the vesical and pelvic plexuses, oviposition may occur in the rectal venules. To maintain the life cycle, the miracidium must find a suitable snail host (*Bulinus* sp.) when it is released from the egg in freshwater. The immature larval worms, after reaching the liver, may migrate via the inferior mesenteric veins to the rectal vein in order to mature. However, they most commonly migrate through the hemorrhoidal and pudendal veins to the vesical and pelvic plexuses. Within 3 months of exposure to cercariae, egg production begins.

Urogenital Disease. Light infections with urinary schistosomiasis usually produce no symptoms; however, in early disease there may be dysuria and hematuria due to cystitis from deposited eggs. Depending on the worm burden, symptoms may include dysuria, frequency, and terminal or total hematuria. Hematuria is so common that in some areas of endemic infection

this phenomenon was considered to be analogous to menarche in girls. Symptoms are usually not seen for 3 to 6 months and may take a year or more to develop. Physical examination is usually normal, but urinalysis may reveal many red blood cells and a few white blood cells on microscopic examination; reagent strip results may indicate hematuria and proteinuria. Chronic disease may lead to major diseases, including obstructive uropathy, chronic bacteriuria, bladder carcinoma, and bladder calcification.

Eggs are most highly concentrated in the tissues of the bladder and lower ureter. As the eggs become trapped in the tissues, granulomas and pseudoabscesses form, leading to fibrosis and ulceration. With extensive fibrosis, the bladder loses its contractility. The urethra frequently is occluded because of hyperplasia, polyp formation, and discharge of purulent debris plugs from the bladder. The ureters are also frequently involved, and obstruction can cause urine reflux, hydronephrosis, retrograde infections, and renal failure. Heavy infections in males may involve the penis, resulting in elephantiasis due to blockage of the scrotal lymphatics by egg deposition. Detection of *S. haematobium* eggs in 43% of semen samples with increased levels of eosinophil cationic protein suggests that the male genital organs are frequently affected.

Up to 75% of women with urinary schistosomiasis have *S. haematobium* eggs in the genitalia; urinary schistosomiasis is associated with sandy patches in the lower genital tract. Eggs have also been detected in biopsy specimens from vaginal mucosa. Female genital schistosomiasis (FGS) is often associated with eggs in the cervix, vagina, and/or vulva, as seen during examination of a wet cervical biopsy specimen crushed between two glass slides. There is significant correlation between the size of the genital lesions and the number of eggs per square millimeter of crushed tissue. Women with FGS also tend to have more tumors in the vulva than do women with schistosomiasis limited to the urinary tract (35). In one study, only 43% of the patients with FGS had hematuria. Also, since FGS frequently exists in women with scanty or no egg excretion in the urine and since this disease represents both an individual and public health hazard in areas of endemic infection, mass treatment targeted to women of childbearing age should be a consideration. *S. haematobium* eggs have been associated with homogeneous yellow sandy patches, mucosal bleeding, and abnormal blood vessels. Genital pathology due to sequestered *S. haematobium* ova is partially reversible 2 to 9 weeks after the adult worms have been killed by praziquantel. A reduction in inflammatory responses can be detected in histologic sections and vaginal lavage fluid. However, these sandy patch

lesions associated with contact bleeding and vessel abnormalities may be refractive to treatment for up to 12 months and may be an important risk factor for potential acquisition and transmission of HIV.

Obstructive Uropathy. Egg deposits in the ureter walls are the general causes of obstructed urinary flow; conditions leading to obstruction include polypoid patches, fibrosis, ureteritis cystica, calculi, and the total number of eggs present. Often these patients remain asymptomatic other than having symptoms related to cystitis or pain from the ureters.

Bladder Calcification. Calcified eggs produce the typical image, which consists of confluent sandy patches. The tissues of the bladder are not calcified and may continue to function normally; however, the visual radiologic picture suggests a heavy infection. Calcified eggs can also be seen in the ureters and seminal vesicles and less often in the colon.

Bladder Carcinoma. Carcinoma of the bladder has been frequently noted in patients infected with *S. haematobium.* Many factors have been suggested as agents promoting schistosome-associated bladder cancer. *N*-Nitroso compounds in association with secondary bacterial infections of the urinary tract may contribute to the high prevalence of bladder cancer. Bladder cancer is the most prevalent cancer in Egyptians. Many of the tumors involve the posterior wall of the bladder and are noted to occur more frequently in males than in females. The extent of *S. haematobium* infection plays a significant role in the induction of different types of carcinoma, since squamous cell carcinoma is usually associated with moderate and/or high worm burdens while transitional cell carcinoma occurs more frequently in areas associated with lighter parasite loads. The predominance of squamous cell carcinoma in urinary bladder tissues in patients with schistosomiasis is probably due to continuous exposure to the larger quantities of carcinogens (*N*-nitroso compounds) in urine in patients with the disease.

Other Body Sites. Periportal fibrosis with hepatomegaly and splenomegaly has been noted in patients in areas where infections are endemic (1). Splenic enlargement has been correlated with the intensity of *S. haematobium* infection. Cardiopulmonary disease can develop in patients with hepatosplenic schistosomiasis; eggs are carried via the mesenteric veins to the lungs through systemic collateral veins. Schistosomal cor pulmonale tends to be rare in infections with *S. haematobium;* and eggs can be found in lung tissue at autopsy but are generally not clinically relevant. Although any *Schistosoma* species may involve the central nervous system, *S. mansoni* and *S.*

haematobium more commonly involve the spinal cord than the brain. Severe disease presents as transverse myelitis.

As with *S. mansoni*, chronic bacteremic infections with *Salmonella* are seen, particularly in cases of chronic active schistosomiasis. Also, schistosomal appendicitis appears to be specific to infection with *S. haematobium* and is an uncommon cause of appendicitis in areas where schistosomiasis is not endemic. Therapy requires antischistosomal medication in addition to surgery.

Diagnostic Procedures. *S. haematobium* eggs are usually detected in the urine, although in heavy infections they may also be found in the stools. The terminal hematuria portion of the urine specimen may contain numerous eggs trapped in the mucus and pus. Peak egg excretion occurs between noon and 3 p.m. Samples collected during this time, or during a 24-h urine collection without preservatives, may be used for examination. Urine can be examined under a microscope after sedimentation or centrifugation. It is important to use saline and not water for the concentration procedures; this will avoid hatching of the eggs. Nuclepore filtration is an excellent method for the concentration of eggs in urine. Some data indicate that egg output in urine is an accurate method of confirming the diagnosis and shows less day-to-day variation than in ELISA detection of schistosome circulating antigens in urine.

Epidemiology and Prevention. *S. haematobium* infections occur in Africa, Asia Minor, Cyprus, islands off the African east coast, and southern Portugal; there is a focus of endemic infection in India. Humans appear to be the only important reservoir hosts, although naturally infected monkeys, baboons, and chimpanzees have been found. The intermediate snail host, *Bulinus* sp., can survive in the mud when the water dries up. The snails retain their infectivity and resume shedding cercariae when the rainy season begins. In some areas, cercariae are found in areas where infected snails are absent, and sometimes cercariae are absent in the presence of infected snails. Data suggest that fewer than 1 in 100 contacts result in infection and less than 1 in 1,000 result in egg output. This suggests that there may be substantial attrition of invading cercariae even in naïve individuals.

References:

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